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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,639	05/21/2001	Doris Huebler	1565	3031

7590 06/04/2004
Michael J Striker
103 East Neck Road
Huntington, NY 11743

EXAMINER

CHANNAVAJALA, LAKSHMI SARADA

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 06/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/806,639

Applicant(s)

HUEBLER ET AL.

Examiner

Lakshmi S Channavajjala

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Receipt of status letter dated 5-10-04 and amendment dated 3-5-04 is acknowledged.

Claims 1-31 are canceled. New claims 32-53 are presented.

New claims 32-44 are directed to a method of manufacturing a bioadhesive tablet comprising embedding testosterone and/or its ester, in an organic polymer, by spray drying process so as to form an amorphous active ingredient premix.

Claims 45-53 are directed to a bioadhesive tablet made by the above process.

Claim Rejections - 35 USC § 103

Claims 32-38 and 45-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Voorspoels et al (Pharmaceutical Research) in view of KR 9606729 (KR).

Voorspoels teaches bioadhesive tablets comprising testosterone and its esters for buccal administration. Testosterone and its esters i.e., acetate, propionate, enanthate and decanoate of Voorspoels meet the claim requirement of testosterone esters with 1-20 carbon atoms in the carboxylic acids radical (page 1228, col. 2, 1st paragraph and table 1).

Instant claim 1 recites testosterone and its esters in an alternate format also i.e., “and/or”. Accordingly, claim 32 can be interpreted as either of the compounds alone and Voorspoels meets the claim requirement because Voorspoels teaches buccal administration of testosterone and testosterone esters separately and not a combination.

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Instant claim 32 recites the method of preparing a tablet by a process of spray drying. Voorspoels fails to teach the claimed process of spray drying.

KR teaches oral adhesive tablet prepared by mixing a pharmacological agent and a polymer such as acrylic acid or hydroxypropyl cellulose, spray drying to prepare micropellets and tableting the micropellets. KR teaches that the tablet has a good adhesive activity and releases the active agent continuously. KR does not teach a specific active agent but teaches the oral adhesive tablet for controlled release of a pharmacological agent. Accordingly, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to prepare the bioadhesive tablet of Voorspoels by employing the method of KR i.e., mixing the drug and the polymer and spray drying to form pellets and tableting the pellets because KR teaches that their process of preparing bioadhesive tablet results in good adhesive activity of the tablet and that the pharmacological constituent of the tablet is released continuously. One skilled in the art would have expected a good adhesion of the bioadhesive tablet of Voorspoels and a continuous and controlled release of testosterone and or its esters contained therein, upon administration. KR does not teach the claimed PVP or HPMC. However, KR teaches hydroxypropyl cellulose, which is also a cellulose derivative liked the claimed HPMC. Therefore, in the absence of criticality of the polymer, choosing an appropriate cellulose polymer with an intention to achieve a good bioadhesion and continuous relelase of active agent would have been within the scope of a skilled artisan.

Further, dependent claims require administration of a mixture of testosterone and testosterone ester in a ratio of 1:100 to 1:1. However, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to combine the optimum amounts of

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testosterone and its esters of Voorspoels in one composition and administer them via buccal route because Voorspoels teaches these compounds independently for simulating the circadian rhythm of testosterone plasma levels. It is obvious to combine two compositions taught by prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose to form a third composition to be useful for the very same purpose. In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069 (CCPA 1980). Accordingly, one of an ordinary skill in the art would have expected to achieve an additive effect in simulating circadian rhythm by combining testosterone and esters of testosterone. Further, Voorspoels studied the bioavailability of buccal tablets in dogs, as opposed to instant claims, which recite a person. However, Voorspoels discussed the various routes of administration of testosterone and its esters, in men, for maintaining circadian rhythm (introduction). Accordingly, it would have been obvious for one of an ordinary skill in the art to administer testosterone and its esters to human beings with an expectation to maintain testosterone levels and stimulate circadian rhythm.

Claims 39-44, 52 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Voorspoels et al (hereafter Voorspoels) and KR 9606729 as applied to claims 32-28 and 45-51 above, and further in view of US 6,063,404 to Timpe et al (hereafter Timpe).

Neither Voorspoels nor KR discussed above, teach a bi-layer buccal tablet. Voorspoels states that the low bioavailability of testosterone esters could be due to the absence of a backing layer and desire a bioadhesive tablet for larger buccal mucosal surface for the absorption of the drug.

Timpe teaches an oral bioadhesive tablet containing at least one bioadhesive adjuvant and at least one lubricant and pharmaceutically active agent. The bioadhesive component is selected from compounds such as cellulose, carboxyvinyl polymer, etc., and lubricant selected from talc, metallic soap, fatty acid mixture etc (col. 3). Further, the tablet is made of 2 layers comprising an active agent layer and a bioadhesive layer. Example 3 (col. 6) particularly recites testosterone ester in the active agent layer. Thus, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to prepare the buccal tablet (containing testosterone and its esters) as a bi-layered tablet by incorporating an adhesive layer over the active agent-containing layer because Timpe teaches that the bioadhesive layer protects the active agent from microbial attack and also provide a large contact area in the buccal mucosa. Accordingly, a skilled artisan would expect to achieve a complete resorption of the active agent (testosterone and its esters) across the oral mucosa because of the bioadhesive layer.

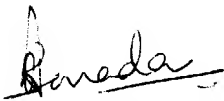
Response to Arguments

Applicant's arguments with respect to rejection of claims over Voorspoels et al and Timpe et al have been fully considered. However, the arguments are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Lakshmi S Channavajjala
Examiner
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May 26, 2004